SESSION 4011

ABPA and Fungal Hypersensitivity of the Upper and Lower Airways

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ABPA

1. Pulmonary Diseases Due to Aspergillus

1. Disseminated aspergillosis
2. Aspergilloma or mycetoma
3. Bronchial asthma
4. Extrinsic allergic alveolitis (malt worker's lung)
5. Allergic bronchopulmonary aspergillosis

2. Diagnostic Criterial for Allergic Aspergillosis

Major Criteria

1. Episodic bronchial obstruction
2. Peripheral blood ecosinophilia
3. Positive immediate skin reactivity
4. Serum precipitating antibodies
5. Elevated serum IgE
6. Elevated IgG and IgE anti-Aspergillus antibodies
7. History of pulmonary infiltrates
8. Central bronchiectasis

Minor Criteria

1. Aspergillus fumigatus positive sputum culture
2. History of expectorating brown plugs or flecks
3. Arthus (late) skin reactivity

3. Similarities of ABPA and CF

Atopy
Asthma
Positive skin test to A. fumigatus
Positive precipitin to A. fumigatus
Elevated IgE
Pulmonary infiltrates
Bronchiectasis

4. % Frequencies or DR and IQ in ABPA

	DR 2	DR 5	DR 2/5	DQ 2
ABPA	**49**	**31**	**74.3**	**20.5**
nonABPA	**16**	**20**	**36.0**	**67.4**
Control	**20**	**14**	**34.7**	**37.7**

5. Treatment of ABPA

A. Prednisone
B. Itraconozole
C. Omalizumab

Allergic Bronchopulmonary Aspergillosis

CHAPTER 43

Raymond G. Slavin

CLINICAL PEARLS

- Allergic bronchopulmonary aspergillosis (ABPA) should be considered in any patient with asthma and pulmonary infiltrates.
- Skin testing with aspergillus is a good screening test for ABPA. A negative skin test essentially rules out the disease.
- Total serum immunoglobulin E (IgE) should reach at least 500 IU/mL before considering ABPA. Most cases are over 1000 IU/mL.
- The increased incidence of ABPA in cystic fibrosis (CF) should prompt yearly determinations of total serum IgE.
- The diagnostic index of suspicion for ABPA in asthma and CF must be high. Early and vigorous treatment is required to prevent the inexorable consequences of bronchiectasis, pulmonary fibrosis, and cor pulmonale.

The inclusion of allergic bronchopulmonary aspergillosis (ABPA) in a text on clinical asthma is quite appropriate. ABPA can be viewed as a complication of bronchial asthma in that it occurs exclusively in asthmatics or in cystic fibrosis (CF) patients who have asthma. It represents a condition in which a basic immunologic disease, bronchial asthma, is complicated by the introduction of another immune response resulting in a different disease entity. The diagnostic index of suspicion of ABPA should remain high, for appropriate therapy must be instituted early enough to prevent irreparable tissue damage.

Aspergillus, the responsible antigen or allergen, is a ubiquitous organism that has been found in air, fertile soil, decayed vegetation and swimming pool water. It is commonly cultured from basements, crawl spaces, bedding, and dust from homes. The specimen of *Aspergillus* that most commonly affects man is *fumigatus*. Pulmonary disease caused by *A. fumigatus* is varied and illustrates how the same organism can elicit different clinical responses, depending on the degree of exposure and the nature of the host. The five types of aspergillus lung disease are:

1. Invasive or septicemic aspergillosis. This condition occurs in individuals with a compromised immune response and is associated with invasion of the bronchial wall resulting in a definite bronchitis. Pneumonia, mycotic abscesses, chronic granuloma, and systemic spread are often seen.
2. Saprophytic aspergillosis or aspergilloma. This is the most common form of aspergillosis and consists of superficial invasion of an anatomic abnormality such as a bronchogenic cyst or a bronchiectatic cavity.
3. Bronchial asthma. *Aspergillus* is one of many molds that can cause immunoglobulin E (IgE)-mediated allergic asthma.
4. Extrinsic allergic alveolitis. This condition is known as malt workers' lung, a form of hypersensitivity pneumonitis due to *Aspergillus clavus* growing in the barley on the floors of breweries.
5. Allergic bronchopulmonary aspergillosis. This condition, described first in 1952, is an example of pulmonary infiltrates with eosinophilia (PIE) syndrome, that is, pulmonary infiltrates with peripheral blood and sputum eosinophilia. Initially thought to be rare in the United States, it is being increasingly reported in this country.[1]

CLINICAL CHARACTERISTICS

History and Physical Examination

Patients with allergic aspergillosis are almost always atopic and have a history of bronchial asthma. Patients complain of anorexia, headache, general aches and pains, loss of energy, temperature elevation, production of solid sputum plugs, and acute attacks of wheezing dyspnea. The disease tends to affect the younger age group, with most cases occurring under the age of 40. Several children have developed the disease before 2 years of age. Most often, no clear relationship can be established between a history of exposure to moldy vegetative matter and the onset of symptoms.

In most patients, there are general signs of airway obstruction, with crepitant rales localized over areas of pulmonary infiltration.

Eosinophilia

Peripheral blood eosinophils are generally over 1000/mm^3, and levels greater than 3000/mm^3 are common.

Sputum

On direct examination of sputum plugs, fungal mycelia are frequently seen with large numbers of eosinophils (Fig. 43-1). A cardinal feature of ABPA is that the organism can actively grow at body temperature shedding antigens and enzymes into the surrounding tissue. The preservation of cytoplasm as seen in Figure 43-1 indicates active growth of the fungus. This is in contrast to the dead mycelia that are devoid of cytoplasmic content as seen in aspergilloma.

A positive sputum culture is not diagnostic of aspergillosis, as aspergillus is commonly inhaled and expectorated by the population at large. By the same token, patients with allergic

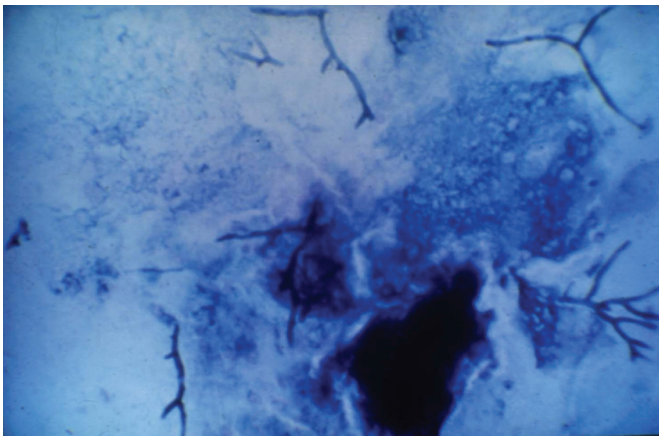

Figure 43-1 Sputum smear of patient with ABPA showing eosinophils with good preservation of cytoplasm, Gomorimethenamine silver stain. *(From Slavin RG: Allergic bronchopulmonary aspergillosis. In Fireman P, Slavin RG [eds]: Atlas of Allergies, 2nd ed. London, Mosby-Wolfe, 1996, pp 131–139.)*

aspergillosis frequently have negative sputum culture during episodes of pulmonary infiltration. The organism can best be grown in Sabouraud's glucose peptone broth or Czapek-Dox medium.

Skin Tests

The presence of a positive immediate wheal and erythema reaction to an aspergillus skin test is a necessary finding in allergic aspergillosis. A negative skin test for all intents and purposes rules out the diagnosis. On the other hand, a positive skin test indicates only the presence of immunoglobulin E (IgE) antibodies to aspergillus and is not diagnostic of allergic aspergillosis. Twenty-five percent of bronchial asthmatic individuals are skin test positive to *A. fumigatus*.

Precipitins

Precipitating antibody of the IgG type to *A. fumigatus* is present in the serum of 69% of patients with allergic aspergillosis. When the serum is concentrated three- to fourfold, the percentage of positive precipitin reactions increases to well over 90%. As in the case of immediate skin reactivity, the presence of precipitating antibody to *A. fumigatus* is not diagnostic of allergic aspergillosis, for it has been demonstrated in 9% of hospitalized patients, 3% of healthy office workers, 12% of allergic asthmatic patients, 27% of patients with farmer's lung, and practically all patients with aspergilloma.

IgE

Serum IgE levels in allergic aspergillosis are generally markedly elevated, being significantly higher than in uncomplicated bronchial asthma. A recent Cystic Fibrosis Consensus Document recommends IgE levels higher than 417 IU/mL or higher than 1000 ng/mL as being consistent with ABPA.

Studies using absorption of serum with *A. fumigatus* antigens indicate that the majority of the total serum IgE in ABPA is not specific for *A. fumigatus*. This nonspecific elevation of total serum IgE is probably due to production of interleukin (IL)-4 by ABPA lymphocytes when they are incubated with *A. fumigatus* in vitro.

The Cystic Fibrosis Foundation has recently suggested that all CF patients have yearly determination of serum IgE.

Imaging Studies

A variety of radiographic abnormalities are present in allergic bronchopulmonary aspergillosis. Most commonly seen is a massive homogeneous shadow without fissure displacement that usually appears in the upper lobes. The shadow may be patchy, triangular, lobar, or oblong, and it frequently shifts from one site to another (Fig. 43-2). A recurrence in the same area suggests previous bronchial damage that may predispose locally to further episodes.

Another frequently seen abnormality is "tramline" shadows, which consist of two parallel hairline shadows extending out from the hilum in the direction of the bronchi. This is thought to represent bronchial wall edema. Parallel line shadows are similar to tramline shadows, but the width of the transparent zone is wider. They appear to be caused by bronchial damage and often appear in areas where homogeneous shadows had previously been observed and then resolved. A bandlike or "toothpaste" shadow represents secretions in a dilated bronchus. After a mucous plug is expectorated, a toothpaste shadow often reverts to a tubular shadow. A gloved ring shadow represents secretions in a dilated bronchus with an occluded distal end, and ring shadows, consisting of a hairlike ring, indicate cavities.

A commonly seen radiographic finding in allergic aspergillosis is atelectasis of a segment, a lobe, or total collapse of the whole lung due to mucous plug occlusion.

It is important to realize that an inconspicuous radiographic appearance can represent extensive tissue damage. The diagnosis of ABPA can be suspected from such a modest finding as a tramline shadow or by residual damage, such as a shrunken upper lobe.

The imaging features described thus far are best identified with computed tomography (CT). CT is far more sensitive than chest radiography for the detection of bronchiectasis. Mucous plugging in large bronchi can be seen on plain radiographs but is more frequently identified by CT. Centrilobular nodules and high-attenuation mucous plugs can be identified only by CT.[2]

Pulmonary Function

In allergic aspergillosis, pulmonary function testing during clinical flares shows significant decline in total lung capacity, vital capacity, forced expiratory volume in 1 second (FEV_1), and carbon monoxide diffusion (DLCO). The decrease in DLCO is probably due to the presence of bronchiectasis and is an extremely important index of disease severity, as uncomplicated bronchial asthma is associated with a normal DLCO. The abnormal pulmonary function tests return toward baseline with remission, and in most patients, no significant functional deterioration occurs with proper treatment after diagnosis.

Bronchial Challenge

The patient with allergic aspergillosis will respond to a bronchial challenge of *A. fumigatus* in a dual fashion.

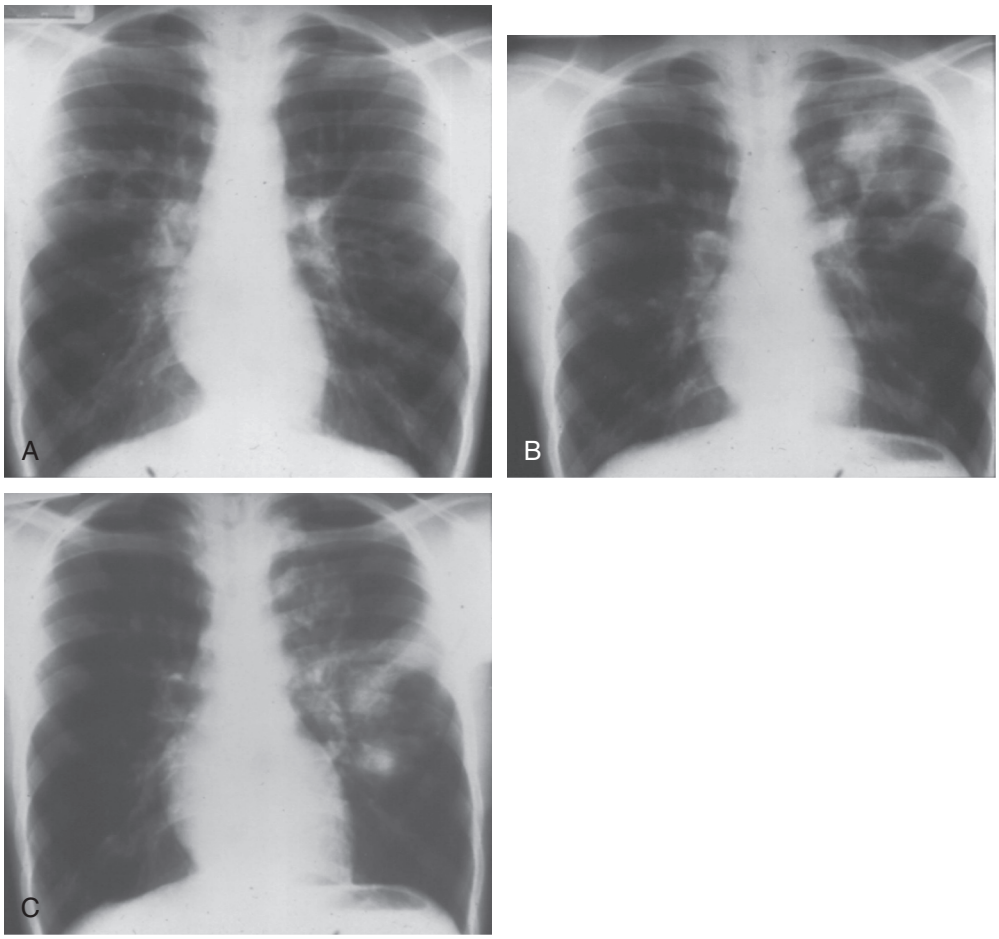

Figure 43-2 Chest radiographs demonstrating fleeting infiltrates in the case of ABPA. A, Soft nodular infiltrates in the right upper lobe suggest tuberculosis. **B,** Fourteen days later, there is some clearing on the right with a new infiltrate present in the left midlung field. **C,** Ten days later, the left midlung has cleared but a new infiltrate is present in the upper lobe. *(From Slavin RG: Allergic bronchopulmonary aspergillosis. In Fireman P, Slavin RG [eds]: Atlas of Allergies, 2nd ed. London, Mosby-Wolfe, 1996, pp 131–139.)*

After an immediate decrease in FEV_1, with subsequent clearing, a late asthmatic reaction occurs at 4 to 6 hours that is associated with fever and leukocytosis. The immediate reaction can be blocked by a beta-agonist. Corticosteroids will prevent the late reaction, and cromolyn blocks both the immediate and late responses.

Lung Biopsy

In an earlier study of lung biopsy in ABPA, the bronchial wall demonstrated infiltration with mixed inflammatory cells, primarily mononuclear cells and eosinophils. Some bronchi were dilated and filled with inspissated mucus and exudate. Fungal hyphae were identified with the exudates but there was no invasion of bronchial wall and lung parenchyma. In areas of lung parenchyma that were extensively consolidated, there were chronic inflammatory cells and large numbers of granulomas, most of which displayed central necrosis, multinucleated giant cells, and a prominent eosinophil infiltrate.

In a later study using newly available immunohistologic techniques, new insights were gained into the pathogenesis of ABPA. Light microscopy revealed a marked inflammatory process that was largely bronchocentric. Elastin layers were intact in blood vessels and markedly disrupted in bronchioles. By immunofluorescence, major basic protein was demonstrated in eosinophils (Fig. 43-3), was freely deposited outside of eosinophils especially in the interlobular septum, and was taken up by macrophages. A number of lymphocytes stained positively for IgE. A significant increase in IL-2 positive staining T cells was observed with an approximate 2:1 ratio of helper to suppressor cells. The most significant finding, demonstrated through an immunoperoxidase stain, was the presence of septate hyphae of aspergillus in the lung parenchyma.[3]

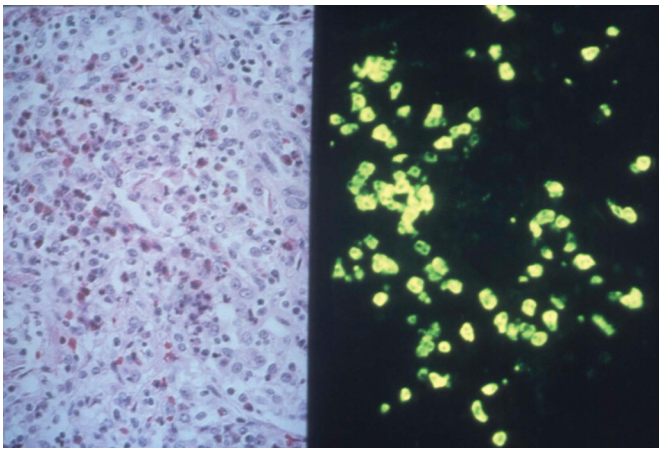

Figure 43-3 Lung biopsy of a patient with ABPA. Hematoxylin and eosin stain is on the left. On the right, the same section is stained with fluorescein-labeled, anti-major basic protein antibody. Positive staining corresponds to eosinophils (×400). *(From Slavin RG, Bedrossian CW, Hutcheson PS, et al: A pathologic study of allergic bronchopulmonary aspergillosis. J Allergy Clin Immunol 1988;81:718–725.)*

DIAGNOSIS

The diagnostic criteria for allergic aspergillosis are shown in Table 43-1. It has been suggested that the presence of the first seven major criteria makes the diagnosis of allergic aspergillosis highly likely, whereas all eight make it certain.[1]

A practical approach to the diagnosis of allergic aspergillosis is seen in Figure 43-4. First, evaluate any patient with a history of pulmonary infiltrates and asthma with an aspergillus skin test. If this is positive, then serum should be checked for a total IgE level and precipitins to *A. fumigatus*.

If the total serum IgE is less than 500 IU/mL, ABPA is highly unlikely. If the IgE is higher than 500 IU/mL then antiaspergillus IgE and IgG should be determined irrespective of precipitins. If these are elevated, then a high-resolution CT of the chest should be obtained to determine the extent of lung involvement.

Asthmatic individuals who require corticosteroids for management might well be a group with underlying allergic aspergillosis. In a study of 42 such patients, 12 were found who were suspect. Of these, three had definite and three had probable allergic aspergillosis. This subgroup is more likely to be younger, to require larger corticosteroid doses, to have a higher incidence of positive skin test to *A. fumigatus* and other antigens, and to have elevated serum IgE levels. It is now recognized that species of aspergillus other than *fumigatus* may be responsible for allergic aspergillosis. In suspected patients whose serum is negative to a battery of *A. fumigatus* antigens, it may be necessary to isolate and extract the strain or species of aspergillus in the patient's sputum to elicit precipitin reactivity. Both *Aspergillus ochraceus* and *Aspergillus terreus* have been shown to cause allergic aspergillosis.

It has been suggested that a staging system can be used for ABPA. Stage I is the acute stage associated with all of the clinical and serologic characteristics of the disease. Stage II is clinical remission in which there are no chest infiltrates or need for prednisone for at least 6 months. Stage III is recurrent exacerbation similar to clinical and x-ray presentation with stage I. Stage IV is steroid-dependent asthma in which there may or may not be subsequent roentgenography infiltrate. Stage IV is end-stage fibrotic disease with irreversible impairment of pulmonary function.[4]

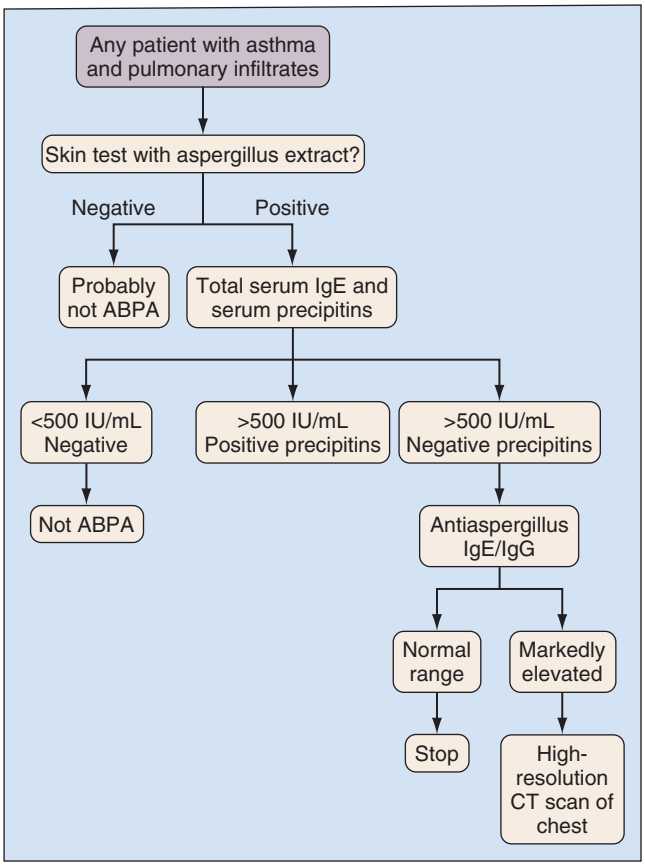

Figure 43-4 Flow diagram of a diagnostic approach to allergic bronchopulmonary aspergillosis. *(From Slavin RG: Allergic bronchopulmonary aspergillosis. In Fireman P, Slavin RG [eds]: Atlas of Allergies, 2nd ed. London, Mosby-Wolfe, 1996, pp 131–139.)*

Table 43-1
DIAGNOSTIC CRITERIA FOR ALLERGIC ASPERGILLOSIS

Major Criteria	Minor Criteria
1. Episodic bronchial obstruction	1. *Aspergillus fumigatus* positive sputum culture
2. Peripheral blood eosinophilia	2. History of expectorating brown plugs or flecks
3. Positive immediate skin reactivity	3. Arthus (late) skin reactivity
4. Serum-precipitating antibodies	
5. Elevated serum IgE	
6. Elevated IgG and IgE anti-Aspergillus antibodies	
7. History of pulmonary infiltrates	
8. Central bronchiectasis	

Data from Slavin RG: Allergic bronchopulmonary aspergillosis. In Fireman P, Slavin RG (eds): Atlas of Allergies, 2nd ed. London, Mosby-Wolfe, 1996, pp 131–139.

DIFFERENTIAL DIAGNOSIS

A number of medical conditions may be associated with asthma and pulmonary infiltrates. The primary diagnostic considerations are bacterial pneumonia, carcinoma, and tuberculosis. The frequently seen radiographic findings in allergic aspergillosis of upper lobe shrinkage and cavitation are particularly suggestive of tuberculosis. Appropriate bacterial study should rule this out.

Mucoid impaction of bronchi is associated with obstruction of proximal bronchi, with large plugs of inspissated mucus and exudates. Fungal hyphae are generally not identified in mucus plugs, and there is usually no evidence of aspergillus hypersensitivity. In contrast to the favorable response seen in allergic aspergillosis, corticosteroids are rarely of benefit in mucoid impaction.

Eosinophilic pneumonia consists of migratory pulmonary infiltrates that are usually accompanied by an excess of eosinophils in the peripheral blood. Cough, anorexia, and weight loss are noted. A characteristic radiographic finding is a peripheral density adjacent to the pleura of pulmonary edema. Lung biopsy shows the alveoli to be filled with eosinophils and large mononuclear cells with an interstitial infiltrate of

eosinophils, lymphocytes, and plasma cells. Etiologic factors include chemicals, helminths, and fungi. When an etiologic diagnosis is not found, the condition is termed cryptogenic or idiopathic pulmonary eosinophilia. Characteristics include marked eosinophilia, predominance in females, with less cough and sputum and less airway obstruction. Chest x-ray shows diffuse bilateral low-density shadows, with no atelectasis, bronchiectasis, or lobar shrinkage. Corticosteroids are quite effective treatment.

Bronchocentric granulomatosis is associated with asthma, mucoid impaction, and presence of noninvasive fungi. The distinctive pathologic lesion is replacement of bronchial epithelium by granulation tissue. Radiologic findings include atelectasis, pneumonic consolidation, bronchiectasis, and bronchiolectasis. Although no sensitizing agent has been identified, an allergic pathogenesis is strongly suspected.

PATHOGENESIS

There is generally no clear relationship between exposure to an environment rich in aspergillus spores and the development of allergic aspergillosis. To be sure, isolated cases have been reported, such as ABPA occurring in a habitual marijuana user whose stock supply of drugs contained a heavy growth of aspergillus. However, the incidence of allergic aspergillosis in urban dwellers with little exposure to moldy hay or grain is every bit as high as that in rural inhabitants. A careful survey of patients with diagnosed allergic aspergillosis shows no higher spore exposure than atopic control subjects. In a study of 131 sugar cane workers who were heavily exposed to *A. fumigatus*, only 2 (1.5%) developed allergic aspergillosis. Thus, a high exposure to aspergillus spores is not necessarily important in the development of allergic aspergillosis, and persistent exposure to high concentrations of the organism may not lead to development of the disease. These studies would tend to indicate that specific host susceptibility is more important to the development of allergic aspergillosis than the extent of exposure to the organism.

The disease process begins with the inhalation and trapping of the short chain spores of *A. fumigatus* in viscid secretions contained in the constricted airways of the asthmatic patient. The size of the spores and the broad range of temperatures at which *A. fumigatus* grows makes this organism uniquely suited for colonization of the human bronchial tree. Most other fungal spores will not survive at human body temperature, but *A. fumigatus* germinates and forms mycelia in the bronchi. Allergic aspergillosis is clearly distinguished from other hypersensitivity responses to inhaled allergens in that the organism grows in the respiratory tract and continually sheds antigens into the tissues. Antigens released from the mycelia combine with the previously mentioned IgE and IgG antibodies to set in motion a chain of immunologic reactions culminating in bronchial wall damage and the surrounding pulmonary eosinophilic consolidation.

Aspergillus itself has profound deleterious effects on defense mechanisms. These include decrease in ciliary beat frequency, impairment of fungicidal proteins, inactivation of complement, interference with phagocytic and killing capacity of phagocytic cells, and release of proteolytic enzymes with elastolytic and collagenolytic activities.

The importance of T lymphocytes in orchestrating the immune response is clearly seen in ABPA. Supernatants obtained from aspergillus-stimulated T cells of CF patients with ABPA cause in vitro allogeneic B cell IgE synthesis. Consistent with these findings, peripheral blood B cells from CF patients with ABPA spontaneously synthesized large amounts of IgE in vitro, which is evidence for polyclonal in vivo IgE B-cell differentiation. CD4+ T cell lines derived from ABPA patients and specific for the immunodominant antigen of aspergillus, Asp f1, revealed that the majority of the lines were of the Th2 phenotype. T cell clones (TCC) specific to the Asp f1 antigen were established from the peripheral blood of ABPA patients and all proliferated in response to Asp f1.[5]

Flow cytometric analysis demonstrated that all of the Asp f1-specific clones were CD3+, CD4+, CD8-, and expressed the αβ T-cell receptor. Measurements of cytokine levels after specific stimulation with Asp f1 revealed a high interleukin 4 (IL-4)/interferon γ (IFN-γ) ratio indicative of a Th2-like pattern of cytokine production.

Following up on the previously stated specific host susceptibility, human leukocyte antigen (HLA) typing of ABPA patients has shown a high incidence of HLA-DR2 with allelic predominance of *1501 and *1503. In addition, the HLA-DQ2 allele appears to confer protection.[6]

ASSOCIATION WITH CYSTIC FIBROSIS

The incidence of allergic aspergillosis appears to be markedly increased in patients with cystic fibrosis. Making the diagnosis of ABPA in these patients is particularly difficult because of the similarities of the two diseases (Table 43-2). In cystic fibrosis, there is an increased frequency of all of the following: atopy (46%), positive skin test to *A. fumigatus* (53%), positive sputum culture and precipitins to *A. fumigatus* (51%), and increased IgE (22%). In addition, the radiographic findings are similar, with hyperinflation, peribronchial inflammatory changes, nodular and branching densities of mucous impaction, atelectasis, predominant upper lobe infiltrates, and bronchiectasis being common to both. The diagnosis of ABPA may be suggested if peripheral blood eosinophils are markedly increased, if the serum IgE is greatly elevated to levels above 1000 IU/mL, and if pulmonary infiltrates do not respond to antibiotics, are transient, and resolve with corticosteroids.[7]

One study explored the hypothesis that the cystic fibrosis transmembrane regulator (CFTR) gene plays a role in ABPA. In 11 individuals who met strict criteria for the diagnosis of

Table 43-2
SIMILARITIES OF ALLERGIC BRONCHOPULMONARY ASPERGILLOSIS AND CYSTIC FIBROSIS

Atopy
Asthma
Positive skin test to *Aspergillus fumigatus*
Positive precipitin to *A. fumigatus*
Elevated IgE
Pulmonary infiltrates
Bronchiectasis

ABPA and had normal sweat electrolytes, one carried two CF mutations and five carried one CF mutation.

PROGNOSIS

In a long-term study of 50 patients with untreated ABPA, all patients followed a chronic course with airway obstruction, recurrent pulmonary consolidation, and in many instances, severe lung destruction. Interestingly, one third of these patients with recurrent pulmonary infiltrates were asymptomatic. Therefore, symptoms may bear no relationship to disease severity and cannot be used as a guide to therapy. The majority of patients with allergic aspergillosis who have early diagnosis and proper treatment will show no significant functional deterioration, as determined by pulmonary function testing.

TREATMENT

The basic aim of therapy in ABPA is to break the vicious cycle in which fungus, trapped in viscid secretions contained in the constricted asthmatic airway, continues to provide large quantities of antigenic and enzymatic material. The clinical presentation of ABPA may be quite subtle and a paucity of symptoms may be associated with quite profound tissue damage. Therefore, early and vigorous treatment is important to prevent the inexorable consequences of bronchiectasis, pulmonary fibrosis, and cor pulmonale.

The cornerstone of treatment is systemic corticosteroids. Once the diagnosis of ABPA is made, corticosteroids must be given in a large enough quantity over a sufficient period of time. A daily dose of prednisone, 60 mg/kg body weight in divided doses, is frequently required to clear the chest radiograph completely in the adult. After radiographic clearing, a single daily dose of 0.5 mg/kg of body weight is given for 2 weeks. At this point, there is a gradual taper to 0.25 mg/kg body weight over a 6-week period. The dose is then switched to 0.5 mg/kg body weight every other day for another 6 weeks and then gradually tapered over a 3-month period. In total, the steroid treatment is given over approximately a 7-month period. During this period, monthly serum IgE levels are obtained. A decrease from the initial, markedly elevated level is always seen. A rise in the serial IgE level, subsequently tested on a monthly basis, should prompt an increase in steroid therapy.

Because of the known beneficial effects of corticosteroids, other important aspects of therapy are often forgotten. Effective removal of fungus from the airway is vital and, therefore, attention to bronchial toilet is extremely important. Bronchodilator therapy must be continued throughout the course of therapy. Particularly in the acute phase, effort should be made to remove the viscid secretions with oral fluids, to avoid ice that may cause reflex bronchospasm, to use expectorants such as potassium iodide or guaifenesin, and to employ aggressive physical therapy and postural drainage. In stubborn cases, bronchial lavage may have to be used. Removal of the nidus of infection will hopefully prevent permanent anatomical, bronchial damage. The majority of patients who receive an early diagnosis and proper treatment will show no significant functional deterioration.

There have been promising reports on the effectiveness of itraconazole, an oral antifungal agent, on decreasing the fungal burden in ABPA. In one study of nine patients treated with prednisone, the addition of itraconazole at a dose of 400 mg daily resulted in a decrease in recurrence of radiographic shadows and a reduction in oral steroid requirement. An open study showed that this approach reduced recurrence of flare-ups, reduced IgE levels and blood eosinophils, and improved FEV_1. In a study of clinically stable ABPA patients, 400 mg daily of itraconazole alone resulted in reduction in sputum eosinophils and eosinophilic cationic protein, total serum IgE, specific IgG to aspergillus, and requirement of oral steroids for respiratory symptoms.[8] At present, itraconazole should be considered add-on therapy to prednisone. Patients should be under a specialist's care for the treatment of ABPA.

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